PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Song, Z. J., Zhao, M. M.		
Serial No.:	To Be Assigned	Case No.: 20818	Art Unit: to be assigned
Filed:	January 22, 2002		Examiner:
For:	PROCESS FOR MAKING SPIRO ISOBENZOFURANONE COMPOUNDS		To be assigned

Assistant Commissioner for Patents
BOX APPLICATIONS
Washington, D.C. 20231

EXPRESS MAIL CERTIFICATE
DATE OF DEPOSIT January 22, 2002
EXPRESS MAIL NO EL523911220US
I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS EXPRESS MAIL "POST OFFICE TO ADDRESSEE" BEFORE 5 P.M. ON THE ABOVE DATE IN AN ENVELOPE ADDRESSED TO ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231.
MAILED BY _____
DATE January 22, 2002

PRELIMINARY AMENDMENT

Sir:

The Examiner is respectfully requested to enter the following Preliminary Amendment in this application under 37 CFR 1.53(b).

IN THE SPECIFICATION

Please add the following section at page 1, before Background of the Invention:

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No. 60/263,463, filed January 23, 2001.

Please delete the paragraph on page 6, line 19 to page 7, line 2 and insert therefore the clean version of the paragraph provided immediately below to read as follows:

To a 100-mL round bottom flask are added toluene (20 mL), water (20 mL), DMF (4.0 mL), K_2CO_3 (4.77 g), 2-amino-5-bromopyrazine **2** (4.30 g) and phenylboronic acid (3.08 g), followed by the catalyst $PdCl_2$•dppf•CH_2Cl_2 (84 mg). The mixture is degassed by a vacuum/N_2 cycle three times, then heated to reflux (~87 °C) until the starting material **2** is less than 1A% by

HPLC (5-8 h). It is cooled to 25 °C, then THF (20 mL) is added to dissolve the product. The organic layer is separated and then washed with brine (20 mL). It is then treated with Darco-KB (600 mg) for 3 hours. The mixture is filtered through a Solka-Floc pad and the filter cake is washed with 1/1 toluene/THF (8.0 mL). The filtrate is concentrated under vacuo to ~16 mL, then heptane (20 mL) is added over ~1 hour and the mixture is aged for 2 hours. The product is collected by filtration and the filter cake is washed with 1/1 toluene/heptane (8.0 mL). It is dried on the funnel to constant weight affording the product **3** as a yellow solid. HPLC conditions: same as in described in the bromination step. RT: phenylboronic acid, 8.0 min (broad), Suzuki product **3**, 9.7 min.

REMARKS

The "Cross-Reference to Related Applications" section was added to allow this non-provisional application to claim the benefit of the filing date of U.S. Provisional Application No. 60/263,463. In the specification, the paragraph on page 6, line 19 to page 7, line 2 was amended to correct a typographical error by substituting the word "weight" for "weigh."

Applicants earnestly request the allowance of Claims 1-11 herein.

Respectfully submitted,

By Baerbel R. Brown

Baerbel R. Brown, Reg. No. 47,449
Attorney for Applicants

MERCK & CO., Inc.
P.O. Box 2000
Rahway, New Jersey 07065-0907
Tel: (732)594-0672

January 22, 2001

VERSION OF AMENDED CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

The paragraph on page 6, line 19 to page 7, line 2, with the markings to show the changes made:

To a 100-mL round bottom flask are added toluene (20 mL), water (20 mL), DMF (4.0 mL), K_2CO_3 (4.77 g), 2-amino-5-bromopyrazine **2** (4.30 g) and phenylboronic acid (3.08 g), followed by the catalyst $PdCl_2$•dppf•CH_2Cl_2 (84 mg). The mixture is degassed by a vacuum/N_2 cycle three times, then heated to reflux (~87 °C) until the starting material **2** is less than 1A% by HPLC (5-8 h). It is cooled to 25 °C, then THF (20 mL) is added to dissolve the product. The organic layer is separated and then washed with brine (20 mL). It is then treated with Darco-KB (600 mg) for 3 hours. The mixture is filtered through a Solka-Floc pad and the filter cake is washed with 1/1 toluene/THF (8.0 mL). The filtrate is concentrated under vacuo to ~16 mL, then heptane (20 mL) is added over ~1 hour and the mixture is aged for 2 hours. The product is collected by filtration and the filter cake is washed with 1/1 toluene/heptane (8.0 mL). It is dried on the funnel to constant ~~weigh~~ weight affording the product **3** as a yellow solid. HPLC conditions: same as in described in the bromination step. RT: phenylboronic acid, 8.0 min (broad), Suzuki product **3**, 9.7 min.